



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: MERCK-3082

In re patent application of

ASFARI, MARYAM et al.

Serial No. 10/553,676

Filed: October 17, 2005

For: INSULIN-INDUCED GENE AS THERAPEUTIC TARGET IN DIABETES

STATEMENT TO SUPPORT FILING AND SUBMISSION IN
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Mail Stop SEQUENCE

Sir:


In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;

2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same.

Respectfully submitted,

Oct. 10, 2006
Date


James A. Coburn

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800-318-3021



STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/553,676
Source: IFWP
Date Processed by STIC: 8/15/06

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebs/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):
U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

Raw Sequence Listing Error Summary

ERROR DETECTED

SUGGESTED CORRECTION

SERIAL NUMBER:

10/553,676

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1 Wrapped Nucleics
 Wrapped Aminos The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."

- 2 Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces.

- 3 Misaligned Amino
 Numbering The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.

- 4 Non-ASCII The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.

- 5 Variable Length Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.

- 6 PatentIn 2.0
 "bug" A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.

- 7 Skipped Sequences
 (OLD RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:
 (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 This sequence is intentionally skipped
 Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

- 8 Skipped Sequences
 (NEW RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence.
 <210> sequence id number
 <400> sequence id number
 000

- 9 Use of n's or Xaa's
 (NEW RULES) Use of n's and/or Xaa's have been detected in the Sequence Listing.
 Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
 In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

- 10 Invalid <213>
 Response Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence. (see item 11 below)

- 11 Use of <220> Sequence(s) missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown."
 Please explain source of genetic material in <220> to <223> section or use "chemically synthesized" as explanation. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32), also Sec. 1.823 of Sequence Rules

- 12 PatentIn 2.0
 "bug" Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

- 13 Misuse of n/Xaa "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid



IFWP

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/553,676

DATE: 08/15/2006
TIME: 12:21:39

Input Set : A:\PTO.RJ.txt
Output Set: N:\CRF4\08152006\J553676.raw

*see item 4 on Error
summary
sheet*

5 <110> APPLICANT: MERCK-SANTE
6 CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS)
9 <120> TITLE OF INVENTION: Insulin-induced gene as therapeutic target in diabetes
13 <130> FILE REFERENCE: BFF 03P0004
--> 17 <140> CURRENT APPLICATION NUMBER: US/10/553,676
--> 17 <141> CURRENT FILING DATE: 2005-10-17
17 <160> NUMBER OF SEQ ID NOS: 8
21 <170> SOFTWARE: PatentIn version 3.1

*Suggestion: consult
Sequence Rules
for VALID
format*
*Does Not Comply
Corrected Diskette Needed*

IGNORED SEQUENCES

73 <210> SEQ ID NO: 2
75 <211> LENGTH: 353
77 <212> TYPE: PRT
79 <213> ORGANISM: Rattus sp.
83 <400> SEQUENCE: 2
85 Met Leu Cys Thr Leu Phe Leu Leu Leu Leu Ala Leu Gly Ile Val Gln
--> 86 1 5 10 15 10
89 Thr Thr Arg Pro Cys Phe Pro Gly Cys Gln Cys Glu Glu Glu Thr Phe
--> 90 20 20 25 30 25 30
93 Gly Leu Phe Asp Ser Phe Ser Leu Ile Arg Val Asp Cys Ser Ser Leu
--> 94 35 40 45
97 Gly Pro His Ile Val Pro Val Pro Ile Pro Leu Asp Thr Ala His Leu
--> 98 50 55 60
101 Asp Leu Ser Ser Asn Arg Leu Glu Thr Val Asn Glu Ser Val Leu Gly
--> 102 65 70 75 80
105 Gly Pro Gly Tyr Thr Thr Leu Ala Gly Leu Asp Leu Ser His Asn Leu
--> 106 85 90 95
109 Leu Thr Ser Ile Thr Pro Thr Ala Phe Ser Arg Leu Arg Tyr Leu Glu
--> 110 100 105 110
113 Ser Leu Asp Leu Ser His Asn Gly Leu Ala Ala Leu Pro Ala Glu Val
--> 114 115 120 125
117 Phe Thr Ser Ser Pro Leu Ser Asp Ile Asn Leu Ser His Asn Arg Leu
--> 118 130 135 140
121 Arg Glu Val Ser Ile Ser Ala Phe Thr Thr His Ser Gln Gly Arg Ala
--> 122 145 150 155 160
125 Leu His Val Asp Leu Ser His Asn Leu Ile His Arg Leu Leu Pro Tyr
--> 126 165 170 175
127 Pro Ala Arg Ala Ser Leu Ser Ala Pro Thr Ile Gln Ser Leu Asn Leu
--> 128 180 185 190
131 Ser Trp Asn Arg Leu Arg Ala Val Pro Asp Leu Arg Asp Leu Pro Leu
--> 132 195 200 205

see pp 1-4

*misaligned
amino acid
numbers. see
item 3
on Error
summary
sheet*

see p.2

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/553,676

DATE: 08/15/2006
TIME: 12:21:39

Input Set : A:\PTO.RJ.txt
Output Set: N:\CRF4\08152006\J553676.raw

```

135 Arg Tyr Leu Ser Leu Asp Gly Asn Pro Leu Ala Thr Ile Asn Pro Gly
--> 136 210 215 220
139 Ala Phe Met Gly Leu Ala Gly Leu Thr His Leu Ser Leu Ala Ser Leu
--> 140 225 230 235 240
143 Gln Gly Ile Leu Gln Leu Pro Pro His Gly Phe Arg Glu Leu Pro Gly
--> 144 245 250 255
147 Leu Gln Val Leu Asp Leu Ser Gly Asn Pro Lys Leu Lys Trp Ala Gly
--> 148 260 265 270
151 Ala Glu Val Phe Ser Gly Leu Gly Leu Leu Gln Glu Leu Asp Leu Ser
--> 152 275 280 285
155 Gly Ser Ser Leu Val Pro Leu Pro Glu Thr Leu Leu His His Leu Pro
--> 156 290 295 300
159 Ala Leu Gln Ser Val Ser Val Gly Gln Asp Val Gln Cys Arg Arg Leu
--> 160 305 310 315 320
163 Val Arg Glu Gly Ala Val His Arg Gln Pro Gly Ser Ser Pro Lys Val
--> 164 325 330 335
167 Val Leu His Cys Gly Asp Thr Gln Glu Ser Ala Arg Gly Pro Asp Ile
--> 168 340 345 350
171 Leu
339 <210> SEQ ID NO: 4
341 <211> LENGTH: 353
343 <212> TYPE: PRT
345 <213> ORGANISM: Homo sapiens
349 <220> FEATURE:
351 <221> NAME/KEY: misc_feature
353 <222> LOCATION: (121)..(121)
355 <223> OTHER INFORMATION: 'Xaa' in position 121 represents Ala or Thr.
357 <400> SEQUENCE: 4
359 Met Pro Trp Pro Leu Leu Leu Leu Ala Val Ser Gly Ala Gln Thr
--> 360 1 5 10 15
363 Thr Arg Pro Cys Phe Pro Gly Cys Gln Cys Glu Val Glu Thr Phe Gly
--> 364 20 25 30
367 Leu Phe Asp Ser Phe Ser Leu Thr Arg Val Asp Cys Ser Gly Leu Gly
--> 368 35 40 45
371 Pro His Ile Met Pro Val Pro Ile Pro Leu Asp Thr Ala His Leu Asp
--> 372 50 55 60
375 Leu Ser Ser Asn Arg Leu Glu Met Val Asn Glu Ser Val Leu Ala Gly
--> 376 65 70 75 80
379 Pro Gly Tyr Thr Thr Leu Ala Gly Leu Asp Leu Ser His Asn Leu Leu
--> 380 85 90 95
383 Thr Ser Ile Ser Pro Thr Ala Phe Ser Arg Leu Arg Tyr Leu Glu Ser
--> 384 100 105 110
387 Leu Asp Leu Ser His Asn Gly Leu Xaa Ala Leu Pro Ala Glu Ser Phe
--> 388 115 120 125
391 Thr Ser Ser Pro Leu Ser Asp Val Asn Leu Ser His Asn Gln Leu Arg
--> 392 130 135 140
395 Glu Val Ser Val Ser Ala Phe Thr Thr His Ser Gln Gly Arg Ala Leu
--> 396 145 150 155 160
399 His Val Asp Leu Ser His Asn Leu Ile His Arg Leu Val Pro His Pro

```

*same
errors*

*misaligned
number*

seq 3

RAW SEQUENCE LISTING
PATENT APPLICATION: US/10/553,676

DATE: 08/15/2006
TIME: 12:21:39

Input Set : A:\PTO.RJ.txt
Output Set : N:\CRF4\08152006\J553676.raw

```
--> 400      165      170      175
403 Thr Arg Ala Gly Leu Pro Ala Pro Thr Ile Gln Ser Leu Asn Leu Ala
--> 404      180      185      190
407 Trp Asn Arg Leu His Ala Val Pro Asn Leu Arg Asp Leu Pro Leu Arg
--> 408      195      200      205
411 Tyr Leu Ser Leu Asp Gly Asn Pro Leu Ala Val Ile Gly Pro Gly Ala
--> 412      210      215      220
415 Phe Ala Gly Leu Gly Gly Leu Thr His Leu Ser Leu Ala Ser Leu Gln
--> 416 225      230      235      240
419 Arg Leu Pro Glu Leu Ala Pro Ser Gly Phe Arg Glu Leu Pro Gly Leu
--> 420      245      250      255
423 Gln Val Leu Asp Leu Ser Gly Asn Pro Lys Leu Asn Trp Ala Gly Ala
--> 424      260      265      270
427 Glu Val Phe Ser Gly Leu Ser Ser Leu Gln Glu Leu Asp Leu Ser Gly
--> 428      275      280      285
431 Thr Asn Leu Val Pro Leu Pro Glu Ala Leu Leu Leu His Leu Pro Ala
--> 432      290      295      300
435 Leu Gln Ser Val Ser Val Gly Gln Asp Val Arg Cys Arg Arg Leu Val
--> 436 305      310      315      320
439 Arg Glu Gly Thr Tyr Pro Arg Arg Pro Gly Ser Ser Pro Lys Val Ala
--> 440      325      330      335
442 Leu His Cys Val Asp Thr Arg Glu Ser Ala Ala Arg Gly Pro Thr Ile
--> 443      340      345      350
446 Leu
491 <210> SEQ ID NO: 8
493 <211> LENGTH: 29
495 <212> TYPE: DNA
--> 497 <213> ORGANISM: Artificial @ primer
--> 501 <220> FEATURE:
--> 501 <223> OTHER INFORMATION:
--> 501 <400> 8
502 gatggaaaga gctcttacat gtgtttatt
--> 504 1
--> 506 P03139 VE
--> 508 1
```

*same
was*

delete
insert <2207 (no response. <2207 is a "header" only)
<223> primer (the explanation! for <213> Artificial Sequence goes in <2207- <223> section, not on <213> line)
move "primer" to <223> line

delete

29

This error also appears in sequences 5 through 7.

from sequence 3

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4

<400> 3

tccagcccc acc atg ccg tgg ccc ctg ctg ctg ctg gcc gtg agt 49

Met Pro Trp Pro Leu Leu Leu Leu Leu Ala Val Ser →

1 3 5 10

(misaligned numbers)

Move amino acids directly

under their codons

the above is a sample of global
error in sequence 3

VERIFICATION SUMMARY

DATE: 08/15/2006

PATENT APPLICATION: US/10/553,676

TIME: 12:21:40

Input Set : A:\PTO.RJ.txt

Output Set: N:\CRF4\08152006\J553676.raw

17 M:270 C: Current Application Number differs, Replaced Current Application No
17 M:271 C: Current Filing Date differs, Replaced Current Filing Date
86 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:2
332 Repeated in SeqNo=2
194 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:3,Line#:190
197 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
201 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
205 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
209 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
213 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
217 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
221 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
224 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:385
225 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
229 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
233 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
237 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
241 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
245 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
249 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
255 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
259 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
263 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
267 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
271 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
275 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
279 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
283 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
287 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:3
360 M:332 E: (32) Invalid/Missing Amino Acid Numbering, SEQ ID:4
332 Repeated in SeqNo=4
387 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4 after pos.:112
456 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:5
459 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:5, <213>
ORGANISM:Artificial Sequence
459 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:5, <213>
ORGANISM:Artificial Sequence
459 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:5,Line#:459
469 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:6
473 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:6, <213>
ORGANISM:Artificial Sequence
473 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:6, <213>
ORGANISM:Artificial Sequence
473 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:6,Line#:473
483 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:7
487 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:7, <213>
ORGANISM:Artificial Sequence
487 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:7, <213>
ORGANISM:Artificial Sequence
487 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:7,Line#:487
497 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:8
501 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:8, <213>
ORGANISM:Artificial Sequence

501 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:8, <213>
GANISM:Artificial Sequence
501 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:8,Line#:501

VERIFICATION SUMMARY

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:504 M:254 E: No. of Bases conflict, this line has no nucleotides.
:506 M:334 E: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:2
:508 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:8